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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/651,846	08/31/2000	Timothy Hla	UCT-0012	4421

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EXAMINER
SCHMIDT, MARY M

ART UNIT	PAPER NUMBER
1635	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/651,846	Applicant(s) HLA ET AL.	
	Examiner Mary Schmidt	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-82* is/are pending in the application.

4a) Of the above claim(s) *41-53,62-72 and 79-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-40,54-61 and 73-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application)

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Genebank* .

File Copy

DETAILED ACTION

1. Newly submitted claims 41-53, 62-72 and 79-82 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: In the Requirement for Restriction mailed, the original claims were restricted among Groups I-IV and Groups VI-X directed to various methods. Applicant elected Group V, drawn to antisense compositions. New claims 33-40, 54-61 and 73-78 fall within the elected Group V, drawn to antisense compositions. New claims 41-53, 62-72 and 79-82 are drawn to methods of using which were originally restricted from the antisense compositions of Group V. These claims are thus considered non-elected and the following claims in Group V will be examined on the merits as drawn to the elected invention: **33-40, 54-61 and 73-78.**

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 41-53, 62-72 and 79-82 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 33-40, 54-61 and 73-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the Official Action mailed 08/28/01.

Applicant's arguments filed 11/29/01, have been fully considered but they are not persuasive.

The new claims are drawn to any antisense oligonucleotide which inhibits the expression of a nucleic acid molecule encoding an EDG-1 or EDG-3 receptor, and antisense oligonucleotide which hybridizes to a nucleic acid molecule encoding an EDG-1 or EDG-3 receptor. These claims are broadly drawn to antisense to EDG-1 or EGD-3 from any species, thus any target nucleic acid which could be called an EDG-1 or EDG-3 gene. Furthermore, the claims as amended are drawn to any possible sequence which hybridizes to any such EDG-1 or EDG-3 sequence.

The specification as filed teaches by way of example specific antisense to EDG-1 and EDG-3 (SEQ ID Nos. 1 and 2 as claimed in claims 35, 56, 74 and 75) which target specific EDG-1 and EDG-3 genes from human (SEQ ID Nos. of the target genes are not provided in the instant specification). However, the specification as filed does not teach by way of sequence target EDG-1 or EDG-3 gene from other whole organisms, accessible regions from such sequences for design of antisense, nor specific sequence structure of nucleic acid sequences which function as

antisense and have the capability to bind and specifically inhibit a particular target EDG-1 or EDG-3 sequence. As argued previously, there is a high level of unpredictability in the antisense art for design of functional antisense absent the sequence structure of the target sequence and knowledge of suitable regions which are open to binding by a particular antisense sequence. The claims are broadly drawn to an undefined genus of nucleic acid sequences which might hybridize to an undefined genus of target EDG-1 or EDG-3 target genes. This breadth, coupled to the unpredictability in the art absent specific sequence information of the target gene and accessible regions and the lack of such teaching in the instant disclosure, leads one skilled in the art to the conclusion that Applicant was not in possession of the scope of the claimed invention at the time the invention was made.

Applicants remarks in the Amendment filed 11/29/01 do not specifically address the 35 U.S.C. 112, written description, rejection made 08/28/01. Thus rejection thus stands as amended to encompass the new claims.

4. Please note that the 35 U.S.C. 112, scope of enablement, rejection is withdrawn in view of the omission of the limitation drawn to *in vivo* use in the new claims.

Claim Rejections - 35 USC § 102

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 33-34, 54-55 and 73 are rejected under 35 U.S.C. 102(a) as being anticipated by Goetzl et al. (J. Of Immunology) for the same reasons of record as set forth in the Official Action mailed 08/28/01.

Applicant's arguments filed 11/29/01 have been fully considered but they are not persuasive.

Claims 33-34, 54-55 and 73 as amended are drawn to: any antisense composition which inhibits the expression of a nucleic acid molecule encoding an EDG-1 or EDG-3 receptor, and any antisense oligonucleotide wherein the antisense oligonucleotide hybridizes to a nucleic acid encoding an EDG-1 or EDG-3 receptor.

Goetzl et al. teach on page 2050, col. 1, 3rd para., nucleic acid primer sequences to EDG-1 and EDG-3 receptors. It is written in the MPEP section 2112.01 that ""products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." Since Goetzl et al. teach compositions having nucleic acid sequences which bind and hybridize in antisense fashion to the claimed target gene, EDG-1 and EDG-3, the claimed antisense are anticipated by Goetzl et al.

Applicant argues that the antisense taught by Goetzl et al. is longer than the dictionary definition of an oligonucleotide. However, in view of the disclosure by Goetzl et al. of antisense oligonucleotides to EDG-1 and EDG-3 as mentioned *supra*, Goetzl et al. does teach the claimed oliogonucleotide compositions.

7. Claims 33-35, 54-56 and 73-75 are rejected under 35 U.S.C. 102(a) as being anticipated by WO9919513/ N_Geneseq_1101 database accession number AAX36573 (July 07, 1999).

Claims 33-34, 54-55 and 73 as amended are drawn to: any antisense composition which inhibits the expression of a nucleic acid molecule encoding an EDG-1 or EDG-3 receptor, and any antisense oligonucleotide wherein the antisense oligonucleotide hybridizes to a nucleic acid encoding an EDG-1 or EDG-3 receptor. Claims 35, 56 and 74-75 further specify an oligonucleotide comprising SEQ ID NO:1 or 2.

WO9919513 teaches an oligonucleotide of 35 bases comprising bases 1-18 of both instant SEQ ID NO:1 and SEQ ID NO:2. It is written in the MPEP section 2112.01 that ""products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." Since the prior art teaches compositions having nucleic acid sequences which bind and hybridize in antisense fashion to the claimed target gene, EDG-1 and EDG-3, comprising instant SEQ ID NO:1 and 2, the claimed antisense are anticipated by the teachings of WO9919513.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 33-40, 54-61 and 73-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goetzl et al. and WO9919513 for the reasons stated above in view of either of Baracchini et al. (U.S. Patent 5,801,154) or Cowsert (U.S. Patent 5,951,455).

Goetzl et al. and WO9919513 are relied upon to teach oligonucleotide compositions having nucleic acid sequences which hybridize to EDG-1 and EDG-3. They do not specifically teach modifications of said sequences nor pharmaceutical compositions of said sequences.

Baracchini et al. and Cowsert et al. are both relied upon to teach design of antisense oligonucleotides to a known gene target and modifications of said antisense for improved function *in vitro*. Specifically, Baracchini et al. teach in cols. 4-10 the motivation to design antisense to a known gene target and methods for modifying said antisense for increased expression. Cowsert et al. teach in cols. 3-12 and 25-32 teach the motivation to design antisense to a known gene target

and methods for modifying said antisense for increased expression. They teach modifications of antisense as follows: modified internucleoside linkage; phosphorothioate linkage; at least one modified sugar moiety; a 2'-O-methoxyethyl sugar moiety; at least one modified nucleobase; a 5-methylcytosine base (Cowsert col. 25-col. 34). They also teach a chimeric oligonucleotide (Cowsert col. 33) and pharmaceutical compositions of the claimed compounds including use of colloidal dispersion systems such as liposomes (Baracchini et al. Col. 4, lines 23-64). They do not specifically teach design of antisense to the EDG-1 or EDG-3 genes as instantly claimed.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to make nucleic acid sequences having an oligonucleotide sequence which binds to EDG-1 or EDG-3 as taught by Goetzl et al. and WO9919513 and having the claimed modifications taught by Baracchini et al. and Cowsert et al.

One of ordinary skill in the art would have been motivated to design nucleic acid oligonucleotide compositions to EDG-1 or EDG-3 since Goetzl et al. taught both design of antisense to EDG receptors as well as the nucleic acid sequences useful for inhibition of EDG gene expression. One of ordinary skill in the art would have been motivated to modify the sequences taught by Goetzl et al. and WO9919513 with the modifications taught by Baracchini et al. and Cowsert et al. for the reasons taught therein, improved stability of the antisense oligonucleotides and improved performance in gene inhibition. One of ordinary skill in the art would have also been motivated to make pharmaceutical compositions comprising the antisense to

EDG-1 or EDG-3 for the reasons taught by Baracchini et al. and Cowsert et al., delivery of the compounds to whole cells, such as those in a whole organism.

One of ordinary skill in the art would have had an expectation of success to make the claimed antisense compositions since oligonucleotide sequences to EDG-1 and EDG-3 were known in the art, and the claimed modifications to said sequences were well-known in the art as taught by Baracchini et al. and Cowsert et al. to improve antisense stability in cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt
February 11, 2002

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